REMARKS

Claims 8-10, 12, 17 and 19 have been amended within the scope of the specification. Claims 13-15 remain as originally drafted reciting additional limitations to dependent Claim 12. Claims 16 and 18 have been canceled. The amendments to the Claims do not represent the inclusion of new matter and are supported by the specification (see for example page 12 lines 15-30 and page 13 lines 1-21).

Response to Rejection of Claims 8-10, 12-19 under 35 USC § 112

Claims 8-10 and 12-19 were rejected under 35 USC § 112, second paragraph, as allegedly indefinite to particularly point out and distinctly claim the subject matter applicant regards as the invention. The Examiner noted that Claim 8 includes the step of determining a spectral range for a modified query peptide and that the specification teaches that a spectral range is the range from zero to the unmodified query peptide's mass. The Examiner stated that the specification did not provide method steps for "determining" the spectral range, accordingly the claims were deemed indefinite.

The current claim amendments, which remove reference to specifically determining a spectral range, are believed to overcome this rejection. In particular, Applicants amended claims recite "identifying a fragmentation spectrum for a sample containing at least one modified query peptide, the at least one modified query peptide having a mass, at least a portion of which is attributable to a modification associated with the at least one modified query peptide" and further that "at least a portion of the fragmentation spectrum comprises mass/charge ratios associated with fragments of the at least one modified query peptide that are distributed over a spectral range ranging from zero to an unmodified mass associated with the modified query peptide."

These amendments are supported throughout the specification including for example at Page 5, Lines 24-29 defining query / fragmentation spectrum and Page 13, Lines 3-25 relating query spectrum and fragmentation mass ratios over selected spectral ranges.

Claim 17 was also rejected under 35 USC § 112, second paragraph for the reason that the term "selected comparison" was not clear. The current claim amendment, which removes reference to the term "selected comparison", is believed to overcome this rejection.

Claims 9-10 were rejected under 35 USC § 112, first paragraph as "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed had possession of the claimed invention." With reference to Claim 9 Applicants have amended the claim to recite "determining a difference mass for the modified query peptide as being the difference between the molecular weight of the modified query peptide and the molecular weight of the unmodified query peptide and further excluding from the analysis fragments associated with the modified query peptide where the difference mass is not known." The determination of the difference mass is defined in the specification at Page 13, Line 3-4. Furthermore, exclusion mass ratios associated with fragments with an unknown difference mass is taught at Page 13, Lines 4-6. Applicant asserts that the clarifications as to what information is being excluded and the basis for the exclusion being a difference mass rather than "modified mass" overcome this rejection. Additionally, Claim 10 has been amended to recite "adjusting mass ratios for fragments associated with the modified query peptide prior to the comparison with fragments associated with known peptide fragmentation spectrum." Adjustment in this manner is taught at Page 13, Lines 13-15. Applicant asserts that the clarifications presented overcome this rejection.

In view of the aforementioned amendments and the teachings present in the specification, a person skilled in the art would recognize that Applicants were in possession of the invention claimed at the

effective filing date of the present application. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

Response to Rejection of Claims 8-10, 12-19 under 35 USC § 102

Claims 8-10 and 12-19 were rejected under 35 USC 102(b) as allegedly being anticipated by Wilkins *et al.* (J. Mol. Biol. (1999) 289, 645-657) or under 35 U.S.C. 102(e) as anticipated by Eriksson *et al.* (US Patent 6,446,010). According to the rejection, "Wilkins *et al.* teach a method of identifying protein post-translational modifications." and further that Wilkins *et al.* teach that "a protein suspected of being modified is subjected to fragmentation" wherein "subjected to fragmentation" is equated to Applicant's teaching of subdivision into a plurality of mass intervals.

Applicant respectfully disagree. Applicant notes that it is not uncommon for proteins / peptides to be modified with respect to the reference protein / peptide in a fragmentation database. For a modified protein / peptide its mass and masses of any modified fragment ions will typically not match that expected from the database. See Application Page 2, Lines 29-30 and Page 3, Lines 1-10. Applicant's invention provides for a modification tolerant search of existing protein fragmentation information. Additionally as discussed in the instant application "the quality of data in a fragmentation spectrum can vary" and conventionally, "searching a peptide database with data derived from a fragmentation spectrum often fails to produce matches with sufficient specificity and sensitivity." See Application Page 9, Lines 14-16. Scoring fragmentation data in the manner claimed by Applicant further provides a significant mechanism by which to categorize the data according to its perceived quality assigning higher weights to higher quality data. See Application Page 9, Lines 16-18 The weights / scoring criteria of the present invention provide a useful way of assaying unknown / modified query spectra to

"improve identification of an unknown query peptide." See Page 11 Lines 21-23.

Conventional methods such as that disclosed by Wilkins *et al.* perform peptide identification fragmentation analysis using significant portions of the fragmentation spectrum referred to as the peptide fingerprint (also known as a peptide map as discussed in the Eriksson *et al.* reference). Wilkins *et al.* disclose that the peptide fingerprint is "constructed by stitching together the spectra from different m/z regions, and calibrating externally with the mass of the parent ion." See Wilkins *et al.* Figure 1 and Page 655 Right Column 1st Paragraph. Using the peptide fingerprint the user "identifies the query protein using available peptide mass fingerprinting search engines" and attempts to account for "peptide masses that did not match with the protein" which "may be due to post-translational modifications" and thereafter applies rules "to make predictions as to which amino acids within the peptide, if any, might carry the modification." See Wilkins *et al.* Figure 1 and Page 646 Right Column "the FindMod Rationale".

Conversely, the peptide modification analysis approach as claimed by Applicant divides the query peptides fragmentation spectrum within the spectral range into separate intervals, with a search performed on each interval postulating that a modification of one or more fragments within the selected mass interval has occurred. See Instant Application Claim 8 and Specification Page 14 Lines 1-3 After performing the searches, scores from each search interval are summed to identify the best match overall. See Instant Application Claim 8 and Specification Page 14 Lines 3-6. Applicant notes that this method increases the sensitivity and specificity of the search by altering the distribution of hits in the search process and goes on to further provide a detailed explanation as to how the hit distribution of the claimed invention differs from a "normal search." See Instant Application Specification Page 14 Lines 7-11 and discussion following.

Based on the foregoing discussion Applicant contends that significant differences exist between the teachings of the present invention and those disclosed by Wilkins *et al.* and that this reference fails to teach the manner of peptide modification analysis claimed by Applicant. It is noted that conventional methods such as that disclosed by Wilkins *et al.* attempt to employ strategies that may be used in modification tolerant searching but bring with them certain drawbacks. For example, it appears that Wilkins *et al.* disclose calculating mass differences between a query peptide and all theoretical peptides that may arise from a modification. See Wilkins *et al.* Figure 1 and associated discussion. One drawback to this approach is that it significantly increases the size of the databases and is less efficient / reliable when dealing with unknown modifications. Accordingly, Wilkins *et al.* does not anticipate any of the claims pending in the instant Application, at least for the reasons discussed above, and the present rejection should be withdrawn.

Applicant further respectfully disagrees with the Examiner regarding the applicability of the Eriksson *et al.* reference. Like Wilkins *et al.*, Eriksson *et al.* fails to teach or suggest the peptide modification analysis approach as claimed by Applicant. More specifically, Eriksson *et al.* does not teach or suggest dividing the query peptides fragmentation spectrum within the spectral range into separate intervals, with a search performed on each interval postulating that a modification of one or more fragments within the selected mass interval has occurred. See Instant Application Claim 8 and Specification Page 14 Lines 1-3 Like Wilkins *et al.*, Eriksson *et al.* also fail to teach or suggest that after performing the interval searches, scores from each search interval are summed to identify the best match overall. See Instant Application Claim 8 and Specification Page 14 Lines 3-6.

As previously noted the method as claimed by Applicant may increase the sensitivity and specificity of the search by altering the distribution of hits in the search process. See Instant

Application Specification Page 14 Lines 7-11 and discussion following. The Examiner asserts that Claims 45 and 47 of the Eriksson *et al.* reference disclose constraining a comparison within a chosen mass range, however, neither these claims nor the specification provide for interval searching and analysis in the manner claimed by Applicant. Accordingly, Eriksson *et al.* does not anticipate any of the claims pending in this application, at least for the reasons discussed above and the present rejection should be withdrawn.

Finally, Claims 8-10, 12-15, 17 and 19 which depend from Claim 8, are believed to be patentable for the same reasons articulated above with respect to Claim 8, and because of the additional features recited therein. Claims 16 and 18 have been canceled and limitations contained therein incorporated into other pending claims.

Response to Provisional Rejection of Claims 8-10, 12-19 for Obviousness-Type Double Patenting

In the Office Action, the Examiner provisionally rejects Claims 8-10, 12-19 under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over claims of Applicant's copending U.S. Patent Application No. 10/241751. The Examiner states that although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the 10/241751 Application are directed to methods for comparing a modified query peptide to a plurality of database peptides.

Applicant respectfully traverses the rejection of the Claims for obviousness-type double patenting because the Claims of the present application are patentably distinct from the claims of U.S. Patent Application No. 10/241751. In particular, pending Claims 8-10, 12-15, 17 and 19 each include the limitation of "apportioning said spectral range for the at least one modified query peptide into a plurality divisions representative of selected mass intervals of the spectral

range" wherein the spectral range relates to a mass range "from zero to an unmodified mass associated with the modified query peptide."

Applicant submits that these limitations are not obvious in view of the claims of the copending application, and respectfully requests that the Examiner withdraw the provisional rejection. However, if the Examiner maintains this provisional rejection, Applicant will consider submitting a Terminal Disclaimer to overcome this rejection upon indication that Claims of the present application are otherwise allowable.

Conclusion

In view of the foregoing remarks, the Applicant submits that the claims pending in the present application are in condition for allowance. A Notice of Allowance is therefore respectfully requested.

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned at 650-638-6932.

Fee Authorization

Should any extension of time and/or fee be necessary for timely submission of this paper, such extension of time is hereby requested, and the Commissioner is hereby authorized to charge **Deposit Account No. 01-2213 (order no. 4928)**. Any deficiency or overpayment should be charged or credited to this deposit account.

Respectfully submitted,

Date: March 13, 2006

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